

WHAT IS CLAIMED IS:

1 1. A method for modulating the plasma circulation half-life of an active
2 agent, said method comprising:
3 (a) providing a liposome having free active agent and precipitated active agent
4 encapsulated therein; and
5 (b) varying the amount of said active agent that is precipitated in said
6 liposome.

1 2. The method of claim 1, wherein step (b) comprises varying said active
2 agent to lipid ratio.

1 3. The method of claim 2, wherein said active agent to lipid ratio is varied
2 by the addition of an empty liposome.

1 4. The method of claim 1, wherein step (b) comprises varying the size of
2 said liposome.

1 5. The method of claim 1, wherein step (b) comprises adding a
2 component that enhances precipitation of said active agent.

1 6. The method of claim 5, wherein said component is a mono-, di-, tri-, or
2 polyvalent anion.

1 7. The method of claim 1, wherein step (b) comprises varying both said
2 active agent to lipid ratio and the size of the liposome.

1 8. The method of claim 1, wherein said active agent is an antineoplastic
2 drug.

1 9. The method of claim 8, wherein said antineoplastic drug is a
2 camptothecin.

1 10. The method of claim 9, wherein said camptothecin is a member
2 selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin, 10,11-
3 methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-piperazino-
4 methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-
5 20(S)-camptothecin.

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- 1 11. The method of claim 10, wherein said camptothecin is topotecan.
- 1 12. The method of claim 1, wherein said active antineoplastic drug is a
2 vinca alkaloid.
- 1 13. The method of claim 12, wherein said vinca alkaloid is a member
2 selected from the group consisting of vincristine, vinblastine, vinorelbine and vindesine.
- 1 14. The method of claim 1, wherein the precipitated active agent
2 encapsulated in said liposome is at least 50% of said total active agent.
- 1 15. The method of claim 14, wherein the precipitated active agent
2 encapsulated in said liposome is at least 60% of said total active agent.
- 1 16. The method of claim 15, wherein the precipitated active agent
2 encapsulated in said liposome is at least 70% of said total active agent.
- 1 17. The method of claim 1, wherein said liposome comprises
2 sphingomyelin and cholesterol.
- 1 18. The method of claim 17, wherein said liposome comprises
2 sphingomyelin and cholesterol in a 55:45 ratio.
- 1 19. The method of claim 1, wherein the plasma circulation half-life of said
2 active agent is modulated for optimum efficacy.
- 1 20. The method of claim 1, wherein the ratio of said active agent to lipid is
2 about 0.005-1:1 (w/w).
- 1 21. The method of claim 20, wherein the ratio of said active agent to lipid
2 is about 0.05-0.9:1 (w/w).
- 1 22. The method of claim 21, wherein the ratio of said active agent to lipid
2 is about 0.1-0.5:1 (w/w).
- 1 23. A method for modulating the plasma circulation half-life of an active
2 agent, said method comprising:

- (a) providing a liposome having free active agent and precipitated active agent encapsulated therein; and
- (b) adding a liposome with no encapsulated active agent.

24. The method of claim 23, wherein the ratio of liposomes containing active agent to liposomes with no encapsulated agent is from about 1:0.5 to 1:1000.

25. The method of claim 24, wherein the ratio of liposomes containing active agent to liposomes with no encapsulated agent is from about 1:1 to 1:100.

26. The method of claim 25, wherein the ratio of liposomes containing active agent to liposomes with no encapsulated agent is from about 1:2 to 1:10.

27. The method of claim 26, wherein the ratio of liposomes containing active agent to liposomes with no encapsulated agent is from about 1:3 to 1:5

28. The method of claim 23, wherein said active agent is an antineoplastic drug.

29. The method of claim 28, wherein said antineoplastic drug is a camptothecin.

30. The method of claim 29, wherein said camptothecin is a member selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin, 10,11-methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-piperazino-methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-20(S)-camptothecin.

31. The method of claim 30, wherein said camptothecin is topotecan.

32. A liposomal formulation, said liposomal formulation comprising:

- a) an antineoplastic drug; and
- b) a liposome having free antineoplastic drug and precipitated antineoplastic drug, wherein the precipitated antineoplastic drug in said liposome is at least 10% of the total antineoplastic drug.

33. The liposomal formulation of claim 32, wherein said antineoplastic drug is a camptothecin.

1 **34.** The liposomal formulation of claim **33**, wherein said camptothecin is a
2 member selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin,
3 10,11-methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-
4 piperazino-methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-
5 isopropylamino)ethyl)-20(S)-camptothecin.

1 **35.** The liposomal formulation of claim **34**, wherein said camptothecin is
2 topotecan.

1 **36.** The liposomal formulation of claim **33**, wherein said antineoplastic
2 drug is a vinca alkaloid.

1 **37.** The liposomal formulation of claim **32**, wherein the free antineoplastic
2 drug and the precipitated antineoplastic drug are different.

1 **38.** The liposomal formulation of claim **36**, wherein said vinca alkaloid is a
2 member selected from the group consisting of vincristine, vinblastine, vinorelbine and
3 vindesine.

1 **39.** The liposomal formulation of claim **32**, wherein the ratio of said
2 antineoplastic drug to lipid is about 0.005-1:1 (w/w).

1 **40.** The liposomal formulation of claim **39**, wherein the ratio of said
2 antineoplastic drug: said lipid is about 0.05-0.9:1 (w/w).

1 **41.** The liposomal formulation of claim **40**, wherein the ratio of said
2 antineoplastic drug: said lipid is about 0.1-0.5:1 (w/w).

1 **42.** The liposomal formulation of claim **32**, wherein said liposome
2 comprises sphingomyelin and cholesterol.

1 **43.** The liposomal formulation of claim **42**, wherein said liposome
2 comprises sphingomyelin and cholesterol in a 55:45 ratio.

1 **44.** The liposomal formulation of claim **32**, further comprising a liposome
2 with no encapsulated active agent.

1 **45.** The liposomal formulation of claim **44**, wherein the ratio of liposomes
2 containing active agent to liposomes with no encapsulated agent is from about 1:0.5 to
3 1:1000.

1 **46.** The liposomal formulation of claim **45**, wherein the ratio of liposomes
2 containing active agent to liposomes with no encapsulated agent is from about 1:1 to 1:100.

1 **47.** The liposomal formulation of claim **46**, wherein the ratio of liposomes
2 containing active agent to liposomes with no encapsulated agent is from about 1:2 to 1:10.

1 **48.** The liposomal formulation of claim **47**, wherein the ratio of liposomes
2 containing active agent to liposomes with no encapsulated agent is from about 1:3 to 1:5.

1 **49.** A liposomal formulation, said liposomal formulation comprising:
2 a) an active agent;
3 b) a liposome having free active agent and precipitated active agent
4 encapsulated therein; and
5 c) an empty liposome.

1 **50.** The liposomal formulation of claim **49**, wherein the ratio of liposomes
2 containing said active agent to said empty liposomes is from about 1:0.5 to 1:1000.

1 **51.** The liposomal formulation of claim **50**, wherein the ratio of liposomes
2 containing said active agent to said empty liposomes is from about 1:1 to 1:100.

1 **52.** The liposomal formulation of claim **51**, wherein the ratio of liposomes
2 containing said active agent to said empty liposomes is from about 1:2 to 1:10.

1 **53.** The liposomal formulation of claim **52**, wherein the ratio of liposomes
2 containing said active agent to said empty liposomes is from about 1:3 to 1:5.

1 **54.** The liposomal formulation of claim **49**, wherein said active agent is an
2 antineoplastic drug.

1 **55.** The liposomal formulation of claim **54**, wherein said antineoplastic
2 drug is a camptothecin.

1 **56.** The liposomal formulation of claim **55**, wherein said camptothecin is a
2 member selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin,
3 10,11-methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-
4 piperazino-methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-
5 isopropylamino)ethyl)-20(S)-camptothecin.

1 **57.** The liposomal formulation of claim **56**, wherein said camptothecin is
2 topotecan.

1 **58.** The liposomal formulation of claim **57**, wherein said antineoplastic
2 drug is a vinca alkaloid.

1 **59.** The liposomal formulation of claim **58**, wherein said vinca alkaloid is a
2 member selected from the group consisting of vincristine, vinblastine, vinorelbine and
3 vindesine.

1 **60.** The liposomal formulation of claim **49**, wherein the ratio of said active
2 agent to lipid is about 0.005-1:1 (w/w).

1 **61.** The liposomal formulation of claim **60**, wherein the ratio of said active
2 agent to lipid is about 0.05-0.9:1 (w/w).

1 **62.** The liposomal formulation of claim **61**, wherein the ratio of said active
2 agent to lipid is about 0.1-0.5:1 (w/w).

1 **63.** The liposomal formulation of claim **49**, wherein said liposome
2 comprises sphingomyelin and cholesterol.